Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Specific antibody response of 14 patients with common variable immunodeficiency to 3 BNT162b2 messenger RNA coronavirus disease 2019 vaccinations

On December 20, 2020, Israel conducted a vaccination campaign against the spread of coronavirus disease 2019 (COVID-19) with a 2-dose regimen of Pfizer-BioNTech messenger RNA vaccine, BNT262b2. By June 1, 2021, 56% of the population was fully vaccinated.[1] The emergence of the highly infectious delta variant and waning of vaccine-elicited immunity contributed to a resurgence in both confirmed and severe illnesses. In June 2021, the number of polymerase chain reaction–confirmed cases increased substantially. Therefore, on July 12, 2021, Israeli authorities decided to administer a third booster dose. Initial studies had indicated that a third BNT162b2 dose increased the antibody neutralization level on average by a factor of 10, and a large-scale real-life study confirmed that a third dose substantially lowered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and disease.[2] This decision was also supported by an observed continuous decrease of anti-S immunoglobulin (Ig)G titers in the overall population and a strong correlation between IgG and neutralizing antibody titers throughout the 6 months following the 2-dose BNT162b2 regimen.[3] This raised an important question: Would patients suffering from primary immunodeficiency disorders of humoral immunity affecting B-cell differentiation and antibody production are also be able to produce effective levels of specific antibodies after receiving a third BNT162b2 dose.

We recently reported our observation that 11 (75%) of 15 patients with common variable immunodeficiency (CVID) produced specific SARS-CoV-2 S1 antibodies in good titers after receiving the second BNT162b2 dose.[4] Those patients were divided into 3 groups, based on the EUROClass, as follows: group B−, total circulating $CD19^+$ B cells less than or equal to 1%; group B+/smB+, total circulating $CD19^+$ B cells more than 1% and switched memory B (smB) cells more than 2%; and group B+/smB−, total circulating $CD19^+$ B cells more than 1% and smB cells less than or equal to 2%. Our data indicated that total circulating $CD19^+$ B cells below the normal range (6%-19%) together with smB cells (≤2%) or total peripheral $CD19^+$ B cells (≤1%) may predict unresponsiveness to BNT162b2. We continued to observe the anti–SARS-CoV-2 spike-specific IgG antibody levels of these patients. We report herein our data including the titers following the third booster or postvaccination infection. Antibody levels were measured using Abbott Architect SARS-CoV-2 S1 IgG assay. Levels greater than 50 AU/mL were considered protective, as previously described.[5] One patient of B+/smB− group started rituximab immediately after receiving the second dose and was excluded from this study; hence, 14 patients were included in this study.

As shown in Table 1, 5 to 6 months after the second dose, specific antibody levels remained nonprotective in all patients from group B−, and those in group B+/smB− with B% cells below 6%. Of the 10 patients who initially responded to the vaccine, only 2 (25%) had unprotective levels. In the other 8 patients, the spike antibody levels ranged between 68.10 AU/mL and 2060.30 AU/mL (median, 152.15). These levels were much lower than reported by a recent study that assessed 122 volunteers for the dynamics of antibody response after a 2-dose BNT162b2 regimen.[5] Six months after the second dose, all participants were reported to have protective levels ranging from 893 to 2463 (median, 1383) (Abbott Architect SARS-CoV-2 S1 IgG assay).

Of our patients with CVID, 2 were diagnosed by polymerase chain reaction with COVID-19 following the second dose: patient (F,30),

Table 1
Cohort Characteristics (n = 14) and Serologic Results for Second and Third Vaccinations and Post–SARS-CoV-2 Infection

Group	Sex	Age (y)	Immunoglobulin levels at diagnosis (mg/dL)			Flow cytometry results		SARS-CoV-2 S1 IgG (AU/mL) after vaccination (dose)			COVID-19 infection	SARS-CoV-2 S1 IgG (AU/mL) after infection
			IgG	IgM	IgA	B%	smB%	14-61 d (dose II)	6-7 mo (dose II)	14-85 d (dose III)		
B−	M[a]	51	104	14	<5	1%		<21	<21	179.4		
(n = 2)	F[a]	30	193	5	14	0%		<21	<21	Refused dose III	Mild, after dose II	NP (45 d)
B+/smB+	M[a]	50	<30	32	195.6	4%	9%	307.3	164.1	1595.30		
(n = 6)	M[b]	72	45.7	61	93.1	3%	14%	300.4	27.5	1622.20		
	M[a]	22	469	21	<5	9%	3%	4924.9	505.20	11,794.20		
	M[b]	81	<30	6	19	2%	10%	58	68.10	228.4		
	F[b]	28	242	35	<5	9%	11%	9708.3	2060.30	9972.90		
	M[a]	61	43.6	15	59.1	11%	7%	2178.3	225.6	2781		
B+/smB−	F[b]	44	99	12	<5	8%	0%	205.7	140.2	223.10		
(n = 6)	F[b]	62	417	20	65	20%	0%	84.6	21.8	231	Mild, after dose III	17,289 (60 d)
	F[a]	48	74	18	<5	8%	2%	625.8	135.6	3454.4		
	F[b]	40	357	6	<5	17%	0%	109.9	121.5	Refused dose III		
	F[a]	38	64	16	<5	4%	1%	<21	<21	Refused dose III	Mild, after dose II	516.1 (60 d)
	F[c]	66	433	21	<5	5%	0%	<21	<21	<21		

Abbreviations: B%, percentage of total circulating CD 19+ B cells as a fraction of lymphocytes; F, female; M, male; NP nonprotective; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; smB%, percentage of IgD-/CD27+/CD19+ switches memory B cells as a fraction of total circulating CD19+ B cells.
Specific antibody test for diagnosis:
[a]absence of isohemagglutinins.
[b]inadequate response to pneumovax-23.
[c]inadequate response to tetanus vaccine.

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from group B−, was diagnosed 6 months following the second dose and presented with mild headache symptoms for 2 days. Her specific antibody levels taken 2 months thereafter remained nonprotective. The second patient (F,38) from group B+/smB− and $CD19^+B$% less than 6% was diagnosed with having COVID-19 6 months after the second dose and presented with mild headache symptoms and fever for 2 days, with seroconversion 2 months after infection (516.10 AU/mL).

Furthermore, 11 patients received the third dose, 10 of whom produced protective antibodies with levels ranging from179 to 9972 AU/mL when measured 14 to 85 days postvaccination. Interestingly, patient (M,51) from group B− did not initially respond but developed a protective level after the third dose, whereas patient F,66 (group B+/smB−) with B% less than 6% remained seronegative after the third dose. Patient (F,62) from group B+/smB− had protective levels after the third dose and was diagnosed by polymerase chain reaction with COVID-19 36 days afterward. She also had mild disease manifestations and her antibody levels increased to 17,289 AU/mL 2 months postinfection.

Although this study is limited by the small cohort, it is the only study to date that made correlations between EUROClass classification and the humoral response to vaccination, and it is the first study to monitor the response of patients with CVID to the third BNT162b2 dose. Hence, our observations may have implications for the future treatment of patients with CVID in the era of COVID-19 pandemic. Patient (F,38) from group B− developed protective specific antibodies only after infection, which confirms the findings of Pulvirenti et al[6] that SARS-CoV-2 infection in patients with CVID causes a more efficient classical memory B cell response than BNT162b2 vaccine. After receiving the 2-dose BNT262b2 regimen, 2 patients were infected by SARS-CoV-2; however, despite having unprotective levels of specific antibodies preinfection, they only developed mild disease. Interestingly, one of our patients (F,30), who maintained to have negative serology result after infection, developed only mild COVID-19 with no post-acute COVID sequelae. This suggests that although the 2-dose BNT162b2 regimen does not increase the humoral response, it may still elicit robust antigen-specific CD8+ and T_H1-type CD4+ T-cell responses.[7] A recent study supports this theory and showed that two-thirds of their vaccinated patients with CVID indeed developed S-peptide–specific T-cell response.[8]

The results of the third BNT162b2 dose suggest that some patients with CVID may need a few BNT162b2 doses to achieve antigen exposure that produces or preserves good humoral response. Therefore, we should consider giving booster doses to patients with CVID earlier than 5 months after the second dose.

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Coronavirus disease 2019–related anxiety is associated with uncontrolled asthma in adults

There is evidence that the coronavirus disease 2019 (COVID-19) pandemic, its mitigation strategies, and resulting life changes are associated with detrimental effects on physical and mental health. Adults in the United States were 3 times more likely to meet the criteria for moderate or serious mental distress in April 2020 than in 2018 (70.4% vs 22.0%).[1] Although there is evidence linking stress with asthma exacerbation,[2] studies addressing the impact of the COVID-19 pandemic on anxiety among adults with asthma are limited. We evaluated the associations of COVID-19–related anxiety with asthma control in adults.

An online, cross-sectional study was conducted with US adults (≥ 18 years old) with a current self-reported physician diagnosis of asthma.[3] Study invitations were shared online (eg, social media, e-mail contacts in the networks of the researchers, ResearchMatch), and participants opted in for an incentive drawing.[3] Anxiety was

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